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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,021	07/27/2006	Claudia Lange	38447-302N01US	9444

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EXAMINER	
KIM, TAEYOON	

ART UNIT	PAPER NUMBER
1651	

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03/15/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,021	LANGE ET AL.	
	Examiner	Art Unit	
	Taeyoon Kim	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,9,11,13,14,16,17 and 19* is/are pending in the application.

4a) Of the above claim(s) *8 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,13,14,16,17 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response filed on 12/18/2009 has been received and entered into the case.

Claims 1-7, 9, 12, 15, 18 and 20 are canceled, claims 8 and 10 are withdrawn from consideration as being drawn to non-elected subject matter, and claims 11, 13, 14, 16, 17 and 19 have been considered on the merits. All arguments have been fully considered.

The claim rejection under 35 U.S.C.§112, 2nd par., has been withdrawn due to the amendment.

Applicant's arguments with respect to claims 11-19 have been fully considered but are moot in view of new grounds of rejections.

It is noted that whether or not the fraction having a density of 1.050-1.070 g/ml contains human mesenchymal stem cells at least 70%, the claimed invention is directed to "**a population of human mesenchymal stem cells**", and the newly entered limitation does not provide structural limitation to the population rather it is directed to the fraction obtainable by carrying out the process steps. Therefore, the teaching of Thiede, directed to a population of human MSCs from human bone marrow, anticipates the claimed invention, and the holding of claim rejection based on Thiede is a must.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11, 13, 14, 16, 17 and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 11 discloses a new limitation directed to the human mesenchymal stem cells making up at least 70% of the fraction. This limitation does not have a proper support from the specification, and hence introduces a new matter to the instant application.

The specification discloses "… the mesenchymal stem cells (or a preparation that contains exclusively or predominantly – i.e. at least 70%, 80% or preferably at least 90%- these cells) obtained according to the method described…" (see p.6 of the specification)

This description cannot be construed that at least 70% of the fraction having a density of 1.050-1.070 g/ml obtained from density gradient centrifugation is human mesenchymal stem cells. Rather, the disclosure of the specification should be interpreted as the cell population obtained by the method results in at least 70% of human mesenchymal stem cells.

Claims 11, 13, 14, 16, 17 and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The current claims disclose that the fraction having a density of 1.050-1.070 g/ml obtained from a density gradient centrifugation of human bone marrow would result in at least 70% of the fraction with human MSCs.

However, the specification does not provide any enabling embodiment for a person of ordinary skill in the art to make such a fraction containing MSCs at least 70% of the fraction.

In the response to the previous OA, Applicant alleged that Thiede teaches the presence of megakaryocyte associated with the mesenchymal stem cells (MSCs) referring Figs. 1 and 2 of Thiede, and concluded that the fractions shown in Thiede must contain at least 50% megakaryocytes. In fact, Thiede discloses the fraction, including one having a density of 1.055 g/ml, would contain a relatively high density of large cells (megakaryocytes) (col. 4, lines 21-23 and 42-45).

If this allegation by applicant is correct, the same analysis should be applicable to the claimed invention raising an enablement issue to the instant application.

This is because the procedure of Thiede is carried out by the same density gradient centrifugation as the claimed method, and the density of the fraction having MSC (i.e. 1.055 gm/ml) is within the range of the claimed invention. Therefore, if MSCs within the fraction of 1.055 gm/ml as taught by Thiede contains at least 50% megakaryocytes, the claimed fraction would have the similar, if not the same, amount of megakaryocytes in the fraction of 1.050-1.070 g/ml of the claimed invention.

Therefore, based on the teaching of Thiede showing highly enriched megakaryotes in the fraction having low density (i.e. 1.055 g/ml), the claimed invention is not considered to enable a person of ordinary skill in the art to obtain a fraction having a density of the claimed range, and having at least 70% of the fraction being MSC.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11, 13, 14, 16, 17 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Thiede et al. (US 5,965,436; IDS ref.).

Thiede et al. teach mesenchymal stem cells obtained from human bone marrow and a pharmaceutical preparation comprising the MSCs combined with a biocompatible carrier suitable for delivering MSCs to the damaged tissue sites (a pharmaceutically acceptable excipient/carrier) (abstract; col. 3, lines 49-60).

Claims 11, 13, 14, 16, 17 and 19 are product-by-process claims. M.P.E.P. § 2113 reads, "Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps."

"Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the

same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

The Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether or not applicants' MSCs differs, and if so to what extent, from the MSCs discussed in Thiede et al. Accordingly, it has been established that the prior art MSCs demonstrates a reasonable probability that it is either identical or sufficiently similar to the claimed MSCs that whatever differences exist are not patentably significant. Therefore, the burden of establishing novelty or unobviousness by objective evidence is shifted to applicants.

Clear evidence that the MSCs of the cited prior art do not possess a critical characteristics (structural distinction) that is possessed by the claimed MSCs would advance prosecution and might permit allowance of claims to applicants' MSCs.

Thus, the reference anticipates the claimed subject matter, or alternatively renders the claimed subject matter obvious.

In the response, Applicant argued that the reference does not teach the new limitation. However, the limitation does not provide any structural limitation to the claimed population of human MSCs rather it is directed to the fraction obtainable by the process steps. Whether or not the fraction contains at least 70% of MSCs, this cannot be considered as a structural limitation to the human MSCs as claimed in the current invention.

Furthermore, Thiede discloses not only 1.073 g/ml fraction but also other lower density fractions including 1.055 g/ml (col. 4) which is within the range of the claimed density.

Nevertheless, the limitation directed to the method steps does not provide any structural limitation to the claimed product.

Applicant alleged that the Examiner did not show a prima facie case of obviousness. It is noted that the claim rejection has been formulated under the combination of 102/103, which has been approved by the courts for product-by-process claims.

M.P.E.P. §2113 states "[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

With regard to the teaching-away argument, the argument is not persuasive. Again, the limitations Applicant relies on are process steps which is not considered as a limiting factor in determining patentability. Furthermore, whether or not the reference requires CD41 antibody to isolate MSCs away from megakaryocytes, the argument is based on features not claimed.

Evidence of secondary considerations, such as unexpected results or commercial success, is irrelevant to 35 U.S.C. 102 rejections and thus cannot overcome a rejection so based. In re Wiggins, 488 F.2d 538, 543, 179 USPQ 421, 425 (CCPA 1973). See M.P.E.P. § 2131.04. Since

the MSCs of Thiede can be isolated from the fraction having a density within the range of the claimed densities, the property of MSCs would inherently be the same as the claimed MSC population.

Therefore, it is the Examiner's position that the current amendment does not provide evidence showing the claimed MSC population has critical characteristics and/or properties that the prior art MSCs do not possess.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taeyoon Kim/
Primary Examiner, Art Unit 1651